

**Original Article**

## A Study to Assess Treatment response and Pattern among Lung Cancer Patients in a Tertiary Care Hospital of India

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**Abstract**

**Introduction:** Lung cancer is among the five main types of cancer leading to overall cancer mortality contributing about 1.3 million deaths/year globally. There are only few Indian studies on bronchogenic carcinoma in patients below 40 years, describing its pattern and epidemiology. Hence we planned this study to assess treatment response and Pattern among Lung Cancer Patients of age less than 40 years and elderly patients.

**Material and Methods:** This was a cross-sectional descriptive study (including retrospective secondary and prospective primary data) using data base of patients of primary lung cancer diagnosed between 1<sup>st</sup> January 2006 to 31<sup>st</sup> December 2012 in indoor and outdoor of department of Respiratory Medicine, J.L.N. Medical College, Ajmer, a tertiary level hospital and teaching center.

**Results:** In the present study there were 1418 male and 352 female patients with male: female ratio of 4.03 suggesting that the disease was more common in males. The maximum number of cases (46.89%) were from the 41-60 year age group followed by (39.21%) in 61-80 years. 9.03% patient were below the age of 40 year. Maximum patients (50%) benefited with partial relief of symptoms and radiological regression after treatment.

**Key Words:** Lung Cancer; Profile; Treatment.

**Introduction**

Lung cancer is among the five main types of cancer leading to overall cancer mortality contributing about 1.3 million deaths/year globally<sup>1</sup>, and it is estimated to rise to more than three million per year by the year 2015. The incidence is increasing globally at a rate of 0.5% per year<sup>2</sup>.

Bronchogenic carcinoma is the most common malignancy in males over 50 years of age but is infrequent under the age of 40 years<sup>3</sup>. Several genetic changes are required for a normal progenitor cell to acquire a neoplastic nature; most human cancers tend to occur after the fourth decade of life. Therefore, lung cancer in patients

aged 40 years or less is uncommon and has characteristics that distinguish it from cancer in older patients, including a higher incidence of adenocarcinoma and a lower male-to-female ratio in young patients.<sup>4</sup>

There are only few Indian studies on bronchogenic carcinoma in patients below 40 years, describing its treatment pattern and response. Hence we planned this study to assess treatment response and Pattern among Lung Cancer Patients of age less than 40 years and elderly patients.

### Material and Methods

This was a cross-sectional descriptive study (including retrospective secondary and prospective primary data) using data base of patients of primary lung cancer diagnosed between 1<sup>st</sup> January 2006 to 31<sup>st</sup> December 2012 in indoor and outdoor of department of Respiratory Medicine, J.L.N. Medical College, Ajmer, a tertiary level hospital and teaching center.

All patients with confirmed histological and cytological diagnosis of bronchogenic carcinoma who attended this department were included in this study. The cases with secondary lung cancer, lymphoproliferative disease, malignant pleural effusion of unknown primary, or nonpulmonary site, sarcomatoid tumors and other rare varieties were excluded from this study. All bed head tickets were retrieved from record section of J.L.N. Hospital to fill the designated proforma of this study.

All cases of bronchogenic carcinoma registered at our institute over last 6 yrs, were scanned in the light of distinctive clinico-radiological features, histological types, evolving trends in the clinical, radiological, histological behavior, response to therapy, patient adherence to treatment and to evaluate their distribution among different age groups. In the present study, we took 40 years as the cutoff age, so as to make sure that there were an acceptable number of younger patients.

This study also provides an overview of aspects of the burden of lung cancer in the elderly in India highlighting certain demographic and epidemiol-

ogical data. In India the normal retirement age is 60 years and also according to various census figures the definition of the elderly, in India is considered above the age of 60 years. Government of India adopted 'National Policy on Older Persons' in January, 1999. The policy defines 'senior citizen' or 'elderly' as a person who is of age 60 years or above.<sup>5</sup> Hence we have taken more than 60 yrs old patients as elderly and above 80 yrs as very elderly.

Following details of patients looked into - name, age, sex, residence, occupation, smoking history including object, duration, smoking index (average number of bidis or cigarettes consumed per day multiplied by the duration of smoking in years)<sup>6</sup>, family history.

Histological type and diagnostic modality by which histopathologic diagnosis was made were recorded from the record section of J.L.N. Hospital. The histological typing based on the accepted system for the clinical staging of lung cancer and the revised international system for lung cancer staging<sup>7</sup>. Those tumors that could not be accurately classified were designated as 'unclassified'. Various modes for tissue procurement are FNAC/ Biopsy of lung, pleural fluid cytology, pleural biopsy, fiber optic bronchoscopy and allied procedure such as bronchial biopsy, brushing, washing, lavage, transbronchial lung biopsy, transbronchial needle aspiration, FNAC / excisional biopsy of lymph node or metastatic sites etc. Diagnostic work up if individualised for further analysis have also been mentioned. The site for FNA / BIOPSY of pulmonary lesion has been decided by clinical sign, x-ray chest with corresponding lateral views, USG and CECT thorax if required.

Pretreatment evaluation included complete clinical history (general as well as respiratory symptoms), physical examination, previous treatment record (chemotherapy or supportive), histopathology and other investigation reports (complete blood count, biochemical studies (RFT, LFT), chest radiograph, ultrasound of abdomen / pelvis, ECG, CT scan of chest) were documented including investigations carried out for staging

and to find out metastasis etc. CT scan of thorax was done in majority of cases. But CT scan of abdomen, brain or other parts of body were done in restricted cases if suggestive symptoms of involvement was there as appropriate due to economic constrains. Chemotherapy and or supportive and symptomatic treatment carried out in the department were noted and response of the treatment were observed and documented. All the documents were compiled with patients database accordingly, and informed written consent was taken from each patient.

According to performance status (ECOG), hematological parameters, cardiac function, liver function, kidney function test, chemotherapy was prescribed and carried out. The patients unfit for chemotherapy were treated symptomatically. After completion of the chemotherapy, the patients were advised for follow up three weekly. All attempts made to stage the disease process as per 7<sup>th</sup> edition of TNM<sup>8</sup> classification based on clinical presentation and available diagnostic tools in resource limited setting & all the data were analyzed statistically by applying chi-square test (epicalc software).

**Results**

**Table 1:** Primary Lung Cancer Patients Year wise Age and Sex Distribution

Year	Male (%)	Female (%)	M : F	Total
2007	206 (82.4)	44 (17.6)	4.68	<b>250</b>
2008	218 (81.9)	48 (18.1)	4.54	<b>266</b>
2009	225 (80.6)	54 (19.4)	4.17	<b>279</b>
2010	233 (78.2)	65 (21.8)	3.58	<b>298</b>
2011	251 (78.19)	70 (21.81)	3.57	<b>321</b>
2012	285 (80.06)	71 (19.94)	4.01	<b>356</b>
<b>Total</b>	<b>1418 (80.11)</b>	<b>352 (19.89)</b>	<b>4.03</b>	<b>1770</b>

Chi-square : 2.87

P-value : 0.719518 (N S)

Year wise primary lung cancer patients both in male and female shows increasing trend.

There is 42.4 % increase in total no. of diagnosed cases between 2007 – 2012 as well as there is increased prevalence among females as suggested by decreasing male: female ratio. (Statistically not significant)

**Table 2:** Primary Lung Cancer Patients Age and Sex Distribution

Age Group	Male (%)	Female (%)	M:F	Total (%)
≤ 40	124 (8.7)	36 (10.2)	3.44	<b>160(9.03)</b>
41-60	663 (46.7)	167 (47.4)	3.97	<b>830 (46.89)</b>
61-80	560 (39.4)	134 (38)	4.18	<b>694 (39.21)</b>
>80	71 (5)	15 (4.26)	4.73	<b>86 (4.86)</b>
<b>total</b>	<b>1418 (80.11)</b>	<b>352(19.88)</b>	<b>4.03</b>	<b>1770</b>

Chi-square : 1.18

P-value : 0.757165 (N S)

In the present study there were 1418 male and 352 female patients with male: female ratio of 4.03 suggesting that the disease was more common in males.

The maximum number of cases (46.89%) were from the 41-60 year age group followed by (39.21%) in 61-80 years. 9.03% patient were below the age of 40 year.

Prevalence of lung cancer was significantly higher among young female (10.23 %) as compared to young male (8.74 %).

There were 1418 male patients with mean age of 58.5 years. Of the 352 female patients, means age was 54.5 years. The mean age at diagnosis in young and old age respectively 34.3 and 60.8. (Statistically not significant)

**Table 3:** Primary Lung Cancer Patients Treatment Response After 4<sup>th</sup> cycle of treatment (n= 453)

Cat.	Response	Cisplatin+ Etoposide (n=379)	Peclitaxel+ Cisplatin (n=74)
I	Complete relief of symptoms, Radiological disappearance	51 (13.4%)	8 (10.8%)
II	Complete relief of symptoms, Radiological regression	158 (41.6 %)	26 (35.1%)
III	Partial relief of symptoms, Radiological regression	190 (50.1 %)	29 (36.7%)
IV	Partial relief of symptoms, Radiologically stable	44 (11.6 %)	8 (10.8%)
V	No relief of symptoms, Radiologically stable	10 (2.6%)	3 (4%)

Chi-square : 1.09

p-value : 0.896558 (N S)

Total 1298 cases were treated by chemotherapy. The patients were evaluated after 4<sup>th</sup> cycle of treatment. Total 453 patients completed 4 cycles and were evaluated.

They were categorized according to symptoms relief, and treatment response. About 13.4% of the patients achieved complete response (symptomatic and radiological) treated with Cis + Eto. and 10.8 % treated with pacli + cis.others benefited with some sorts of symptomatic improvement. Maximum patients (50%) benefited with partial relief of symptoms and radiological regression. Around 2-4 % patients had stable disease. (Statistically not significant)

**Table 4:** Primary Lung Cancer Patients Defaulters From Planned Treatment

Time duration	Once (%)	Twice (%)	More than twice (%)
>2 weeks – 1month	54(20)	49 (18.2)	24 (8.9)
>1m – 2m	43 (15.9)	27 (10)	13 (4.8)
>2m	35 (13)	19 (7)	5 (1.8)
<b>Total</b>	132 (47.3)	95 (35.1)	42 (15.6)

Chi-square : 6.03  
P-value : 0.196757 (non significant diff)

Patients who delayed next cycle by more than 2 weeks were defined as defaulter.

Total 269 (20.7%) patients defaulted from planned treatment and most of them ultimately drop-out from chemotherapy cycles.

Intercycle delay of 2 weeks – 1m commonly seen.

**Table 5:** Primary Lung Cancer Patients Drop-Out From Chemotherapy Between Different Cycles

Cycle	No. of dropout patients (%)	No. of patients received next cycle (n=1298 for I cycle) (%)
I - II	495 (38)	803 (61.8)
II – III	260 (32.3)	543 (41.8)
III – IV	90 (16.5)	453 (34.8)
IV – V	105 (23)	348 (26.8)
V - VI	127 (36.5)	221 (17)

Chi-square : 101.72  
P-value : 0.000001 (highly significant diff)

Maximum no. of patients dropped-out after I and V cycle, and least drop-out rate seen after III cycle. 453 (34.8%) patients completed IV cycle of

chemotherapy. 221 (17 %) patients completed all 6 cycle.

Around 100 patients were telephonically interviewed and asked for reasons for dropped-out registered over last 1 year at our institute. Seriousness of illness, financial constraints, Traditional treatment, symptoms relief and Poor excess to transport were the common reasons.

Around 12 % patients were died before next appointment and some sort of patients with good socioeconomic status took treatment from higher center.

**Table 6:** Primary Lung Cancer Patients Common Reasons For Default

Reasons	Defaulter (no. of patients)	percentage
Debilitating health	78	(29 %)
Forgotten appointment	59	(22 %)
Work commitment	89	(33 %)
Poor excess to transport	43	(16 %)
No relative available	35	(13 %)
Traditional treatment	35	(13 %)
Treatment at other center	48	(18 %)
Side effect of therapy	35	(13 %)
Relief from symptoms	56	(21 %)

Patients who defaulted most commonly gave reasons of work commitment (33 %), debilitating health (29%) and forgotten appointment (22%).

Poor excess to transport, No relative available, Side effect of therapy and Relief from symptoms are the other reasons.

**Discussion**

The present cross-sectional descriptive study (including retrospective secondary and prospective primary data) of one thousand seven hundred seventy (1770) cases of bronchogenic carcinoma, carried out in the department of respiratory medicine, J.L.N. Medical Collage and Associated Groups of Hospitals at Ajmer.

All cases of bronchogenic carcinoma registered at our institute over last 6 years extending from January 2007 to December 2012, were scanned in the light of distinctive clinico-radiological features, histological types, evolving trends in the clinical, radiological, histological behavior, response to therapy and to evaluate their distribution among different age groups. From our extensive search and literature review, we did not find any similar study looking at distribution among different age groups including > 80 yrs age group patients, among lung cancer patients.

In the present study, 160 out of 1770 patients (9.03%) with bronchogenic carcinoma seen at our tertiary care center were 40 years old or younger at diagnosis. Other Indian studies on bronchogenic carcinoma have also found a similar proportion of young ( $\leq 40$  years) patients, the figures reported ranging from 9 to 14%<sup>9,10,11,12</sup>. The proportion of young patients of bronchogenic carcinoma as per the Indian cancer registry ranges from 4.1 to 10%<sup>[13]</sup>. The problem when comparing earlier studies on lung cancer with the Indian cancer registry is the difference in the definition of 'young' (table-2). In the present study, we took 40 years as the cutoff age, so as to make sure that there were an acceptable number of younger patients.

In the present study there were 1418 male and 352 female patients with male: female ratio of 4.03 suggesting that the disease was more common in males. Other studies showing higher proportion of females among younger patients were conducted in western populations and they may be explained partly by the fact that a high percentage of young women smoke in western countries.

Although the definitive treatment of lung cancer is surgical, but often this is not possible as most lung cancers are nonresectable when first diagnosed<sup>2</sup>. In view of early dissemination of SCLC, surgery is generally not feasible, even in the absence of positive radiological and other finding. For NSCLC, surgical resection is the main stay for treatment whenever clinically feasible. Stage I and II disease are operable. According to Belani and Ramanathan<sup>14</sup>, fewer than 15% of all NSCLC

patients are candidates for surgical resection. In the present study surgery was advised in all operable cases of lung cancer but it was refused by the patients and none of them opted for surgery.

Chemotherapy is the corner stone of treatment for SCLC. Standard chemotherapeutic regimens have consistently produced 68-71% response rate in limited stage SCLC and 38-65% response rate in extensive stage SCLC. Katsuya Fujimori et al<sup>15</sup> reported response rate of complete response in 22.7% and partial response in 72.7% by chemotherapy. Bonnie Glisson et al<sup>123</sup> observed complete response in 17% and partial response in 76%, with overall objective response rate of 93% by combination chemotherapy in 33 patients.

In the recent years, chemotherapy has emerged as a viable option in the treatment of NSCLC. The most impressive and widely confirmed evidence for this is the fact that chemotherapy can eradicate NSCLC micrometastasis<sup>16</sup>. In stage IIIB NSCLC, combined chemotherapy and radiotherapy have small benefit over radiotherapy alone. For patients with metastatic disease (stage IV) a number of meta analysis have shown a modest improvement in survival with chemotherapy compared to the best supporting care<sup>17</sup>. In pre-cisplatin era (before 1980 ) response rate was < 20% and in cisplatin era, response rate between 20 to 40 % was noted for NSCLC by chemotherapy<sup>16</sup>. In our study chemotherapy was offered in total 1298 cases. The patients were evaluated after 4<sup>th</sup> cycle of treatment. Total 453 patients completed 4 cycles and were evaluated. They were categorized according to symptom relief, and treatment response. About 13.4% of the patients showed complete response (symptomatic and radiological) treated with Cis + Eto. and 10.8 % treated with pacli + cis. Others benefited with some sorts of symptomatic improvement. Maximum patients got benefit with partial relief of symptoms and radiological regression. Around 2-4 % patients had stable disease. Our results are comparable with the study by Parveen Shahida Akhtar et al<sup>18</sup>, in Bangladesh shown 10% of the patients showed complete symptomatic relief, weight gain

and radiological disappearance of tumor and almost all patients benefited with some sorts of symptom relief.

There were only fewer studies ever published on defaulter rate among patients with cancer namely colorectal and breast cancer, which reported that the defaulter rate ranged from 15 to 21%.<sup>19-21</sup> In our study, the defaulter rate among lung cancer patients was 20.7%. On extensive literature search and review, we could find only few studies addressing defaulters among lung cancer patients. In our study Patients who delayed next cycle by more than 2 weeks were considered as defaulter. Total 269 (20.7%) patients defaulted from planned treatment and most of them ultimately drop-out from chemotherapy cycles. Intercycle delay of 2 weeks to 1 month was commonly seen. This is comparable with the study from Malaysia by T. H. Ng et al<sup>22</sup>, who reported 21.2 % default rate but did not mention any drop-out. A study conducted in Singapore by Lee *et al* on predictor of failed attendance in a multi-specialty outpatient centre in which 22864 patients were recruited. Their defaulter rate was 39%<sup>23</sup>. Elderly people are under-represented in clinical trials and also may not receive appropriate and complete treatment, possibly due to the pessimism of the doctors, patients and their relatives regarding treatment relevance and toxicity in elderly patients<sup>24</sup>. In the recently published SEER database<sup>25</sup>, only 25.8% of the 21,285 patients aged >65 years diagnosed with NSCLC between 1997 and 2002 received first-line chemotherapy.

Patients who defaulted most commonly gave reasons of work commitment, debilitating health and forgotten appointment. Poor access to transport, no relative available, side effect of therapy and relief from symptoms are the other reasons. Vernon *et al.*<sup>26</sup> and Wong *et al.*<sup>27</sup> have reported that younger age group of below 40 years had higher rate of default.

To summarize, we had tried to get admitted all patients suspected to have bronchogenic carcinoma for complete evaluation and to start treatment once diagnosis was confirmed. According to performance status, hematological

parameters, cardiac function, liver function, kidney function test, chemotherapy was prescribed and carried out. The patients unfit for chemotherapy were treated symptomatically. After completion of the chemotherapy, the patients were advised for follow up three weekly. Those who were critically ill, only supportive and symptomatic care were advised whenever they faced the deteriorating sign symptoms. In our study, we noticed that a proportion of patients who were provisionally diagnosed with lung cancer did not turn up for follow-up appointments after initial investigations. Some patients that came for follow-up refused chemotherapy and/or radiotherapy. Some patients even sought traditional treatment. But we had tried our best to give at least I cycle to admitted patients.

In present study maximum no. of patients dropped-out after I and V cycle, and least drop-out rate seen after III cycle. 453 (34.8%) patients completed IV cycle of chemotherapy. 221 (17 %) patients completed all 6 cycle. This higher absentee rate was probably a result of patient's negative perception toward the survival benefit of chemotherapy in advanced lung cancer. Seriousness of illness, financial constraints, traditional treatment, symptoms relief and poor access to transport were the common reasons for abstinence. Parveen Shahida Akhtar *et al.*<sup>18</sup> from Bangladesh also noted about one-third of male and 45% of female patients drop out after first and second visit due to advanced stage, poor performance status and poor socioeconomic condition.

Patients who fail to attend follow-up appointments are a source of disappointment and puzzlement for treating physician. Drop-out and default may result in delaying the appropriate treatment, which affect outcomes and even mortality. The findings will allow clinicians and administrators to take into consideration those factors associated with defaults and drop-out when scheduling follow-up appointments.

### Conclusion

This study was done to assess treatment response and pattern among Lung Cancer Patients. It gives

future direction to researcher to conduct more studies in same domain to produce data which may help in prevention and control of this creeping malady.

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**Conflict of interest:** None

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